2. (**Thrice Amended**) A method for treatment or prophylaxis of toxin-induced peripheral neuropathy, comprising systemically administering to the patient an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective to treat or prophylactically treat toxin-induced peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is identical to SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to the N-terminal amino acid residue.

6. (**Thrice Amended**) A method for the treatment or prophylaxis of virally induced peripheral neuropathy comprising systemically administering to a patient in need thereof an effective amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties sufficient to treat or prophylactically treat virally induced peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is identical to SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to the N-terminal amino acid residue.

10. (**Thrice Amended**) The method of claim 2 or 6, wherein the *hedgehog* amino acid sequence is encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to at least one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6.

11. (**Thrice Amended**) The method of claim 10, wherein the *hedgehog* amino acid sequence is a vertebrate *hedgehog* polypeptide.

13. (**Thrice Amended**) The method of claim 10, wherein the polypeptide includes at least a 50 amino acid extracellular portion of a vertebrate *hedgehog* polypeptide selected from at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15.

14. (**Thrice Amended**) The method of claim 10, wherein the polypeptide includes at least a 150 amino acid extracellular portion of a vertebrate *hedgehog* polypeptide selected from at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15.

15. (**Thrice Amended**) The method of claim 10, wherein the polypeptide includes at least an extracellular portion of a vertebrate *hedgehog* polypeptide corresponding to residues 24-194 of SEQ ID No:15.

19. (**Amended**) The method of claim 10, wherein the polypeptide is modified with one or more fatty acid moieties.

20. (**Reiterated**) The method of claim 19, wherein each fatty acid moiety is independently selected from myristoyl, palmitoyl, stearoyl, or arachidoyl.

21. (**Amended**) The method of claim 10, wherein the polypeptide is modified with one or more aromatic hydrocarbons.

22. (**Reiterated**) The method of claim 21, wherein each aromatic hydrocarbon is independently selected from benzene, perylene, phenanthrene, anthracene, naphthalene, pyrene, chrysene, or naphthacene.

23. (**Amended**) The method of claim 10, wherein the polypeptide is modified one or more times with a C7 - C30 alkyl or cycloalkyl.

30. (**Amended**) The method of claims 2 or 6, wherein the *hedgehog* agonist mimics *hedgehog* signal transduction by altering the localization, protein-protein binding and/or enzymatic activity of an intracellular protein involved in *hedgehog* signaling.

31. (**Amended**) The method of claims 2 or 6, wherein the *hedgehog* agonist alters the level of expression of a *hedgehog* protein, a *patched* protein or a protein involved in *hedgehog* signal transduction.

41. (**Amended**) The method of claims 2 or 6, wherein the patient is being treated prophylactically.

46. (**Amended**) The method of claim 2, wherein the toxin-induced neuropathy is due to contact with a chemotherapeutic agent.

51. (**Thrice Amended**) The method of claim 10, wherein the polypeptide is a fusion protein.

55. (**Twice Amended**) The method of claim 10, wherein the N-terminal fragments have a molecular weight of about 19 kD.

The amended claims are re-stated below to reflect changes with respect to the last filing.

2. (**Thrice Amended**) A method for treatment or prophylaxis of toxin-induced peripheral neuropathy, comprising systemically administering to the patient an amount of a *hedgehog* polypeptide modified with ~~two~~ one or more lipophilic moieties effective to treat or prophylactically treat toxin-induced peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is ~~at least 80%~~ identical to ~~at least one of~~ SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of ~~two~~ one or more lipophilic moieties to ~~an~~ the N-terminal amino acid residue.

6. (**Thrice Amended**) A method for the treatment or prophylaxis of virally induced peripheral neuropathy comprising systemically administering to a patient in need thereof an effective amount of a *hedgehog* polypeptide modified with ~~two~~ one or more lipophilic moieties sufficient to treat or prophylactically treat virally induced peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is ~~at least 80%~~ identical to ~~at least one of~~ SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-

terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of ~~two~~ one or more lipophilic moieties to ~~an~~ the N-terminal amino acid residue.

10. (**Thrice Amended**) The method of claim 2 or 6 ~~9~~, wherein the *hedgehog* amino acid sequence is encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to at least one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6.

11. (**Thrice Amended**) The method of claim 10 ~~9~~, wherein the *hedgehog* amino acid sequence is a vertebrate *hedgehog* polypeptide.

13. (**Thrice Amended**) The method of claim 10 ~~9~~, wherein the polypeptide includes at least a 50 amino acid extracellular portion of a vertebrate *hedgehog* polypeptide selected from at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15.

14. (**Thrice Amended**) The method of claim 10 ~~9~~, wherein the polypeptide includes at least a 150 amino acid extracellular portion of a vertebrate *hedgehog* polypeptide selected from at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15.

15. (**Thrice Amended**) The method of claim 10 ~~9~~, wherein the polypeptide includes at least an extracellular portion of a vertebrate *hedgehog* polypeptide corresponding to residues 24-194 of SEQ ID No:15.

19. (**Amended**) The method of claim 10 ~~16~~, wherein the polypeptide is modified with one or more fatty acid moieties.

21. (**Amended**) The method of claim 10 ~~16~~, wherein the polypeptide is modified with one or more aromatic hydrocarbons.

23. (**Amended**) The method of claim 10 ~~16~~, wherein the polypeptide is modified one or more times with a C7 - C30 alkyl or cycloalkyl.

30. (**Amended**) The method of ~~any of~~ claims 2 or 6 ~~1-6~~, wherein the *hedgehog* agonist mimics *hedgehog* signal transduction by altering the localization, protein-protein binding and/or enzymatic activity of an intracellular protein involved in *hedgehog* signaling.

31. (**Amended**) The method of ~~any of~~ claims 2 or 6 ~~1-6~~, wherein the *hedgehog* agonist alters the level of expression of a *hedgehog* protein, a *patched* protein or a protein involved in *hedgehog* signal transduction.

41. (**Amended**) The method of ~~any of~~ claims 2 or 6 ~~4-6~~, wherein the patient is being treated prophylactically.

46. (**Amended**) The method of claim 2 ~~44~~, wherein the toxin-induced neuropathy is due to contact with a ~~toxic~~ chemotherapeutic agent.

51. (**Thrice Amended**) The method of claim 10 ~~9~~, wherein the polypeptide is a fusion protein.

55. (**Twice Amended**) The method of claim 10 ~~9~~, wherein the N-terminal fragments have a molecular weight of about 19 kD.

REMARKS

Claims 1-73 are the pending claims in the present application. Applicants will cancel non-elected claims upon indication of allowable subject matter. Please cancel, without prejudice, claims 1, 3, 4, 5, 9, 17, 18, 44, 45, 47, 48, 50, 52, 53, and 59-73. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

1-4. Applicants note with appreciation that the request for a Continued Prosecution Application is acceptable, and that the amendments put forth in Paper 28 have been entered in full.